



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
-----------------	-------------	----------------------	---------------------	------------------

10/525,152

02/18/2005

Roger Alberto

1582 WO/US

5284

7590

07/23/2008

Mallinckrodt Inc.
675 McDonnell Boulevard
PO Box 5840
Hazelwood, MO 63134

EXAMINER

GROSS, CHRISTOPHER M

ART UNIT

PAPER NUMBER

1639

MAIL DATE

DELIVERY MODE

07/23/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/525,152	Applicant(s) ALBERTO ET AL.	
	Examiner CHRISTOPHER M. GROSS	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 January 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 15-17, 20-28 and 32-36 is/are pending in the application.
- 4a) Of the above claim(s) 25, 26 and 35 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 15-17, 20-24, 27, 28, 32-34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Responsive to communications entered 1/9/2008 and 4/30/2008. Claims 15-17,20-28,32-36 are pending. Claims 25,26,35,26 stand withdrawn. Claims 15-17,20-24,27,28, 32-34 are examined herein.

Election/Restrictions

Applicant argues, see p 6 section 2 (1/9/2008), that claims 25 and 26 were indicated as reading on the elected species and invention in the response entered 9/4/2007.

In this vein, the examiner notes the following.

(i) While it is indeed indicated by applicant that claims 25 and 26 are readable on the elected species in the response entered 9/4/2007, said response does *not* indicate claims 25 and 26 as readable on the elected invention. Commensurate with current office policy if claims are added after the election, applicant must indicate which of these claims are readable upon the elected invention.

(ii) Applicant's election of a solid-phase bound organic compound wherein the solid support is polystyrene/polyethylene glycol resin, R1 is a metal coordinating group with a biologically active molecule; R2 is a metal coordinating group; R4=R5=H; L is a single bond; and the biologically active molecule is a pharmaceutically active small molecule (biotin) is again acknowledged. In this regard, the examiner most respectfully submits that once the solid phase bound organic compound (starting material), shown as formula (I) in claim 15, substituted as above, comes in contact with a solution of one of the metal complexes set forth in claims 25 and 26, a new non-obvious compound (product) is formed having a different empirical formula, structure and physiochemical

properties. Notably, said product that does NOT read on the elected species of solid-phase bound organic compound (starting material).

For the reasons, set forth above, claims 25 and 26 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 9/4/2007.

Applicant's election with traverse of ^{99m}Tc for the species of Metal in new claim 35 in the reply filed on 4/30/2008 is acknowledged. The traversal is on the ground(s) that the metals set forth in claim 35 belong to an art-recognized class of compounds commonly employed as radiopharmaceuticals. This argument is deemed persuasive, and the restriction requirement mailed 4/15/2008 is hereby vacated.

It is noted, however, newly submitted claims 35-36 directed to an invention that is independent or distinct from the invention originally claimed for the same reasons set forth above regarding claims 25 and 26.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 35-36 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Priority

The present case filed 2/18/2005 is a 371 of PCT/US03/27665 filed 9/2/2003.

To clarify the record, it should be noted that *the examiner* has personally retrieved a **non**-certified copy of European application (EPO) 02078743.8 from the international bureau, to which the present case claims foreign priority under 35 U.S.C. 119(a)-(d).

Acknowledgment is again made of applicant's claim for foreign priority based on an application filed in Europe on 09/03/2002. It is noted, however, that applicant has not officially filed an certified copy of the European application as required by 35 U.S.C. 119(b).

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the prior application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Prods., Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994) [taken from MPEP 201.01]

The present application, filed 2/18/2005 claims priority as a 371 of PCT/US03/27665 filed 09/02/2003 and further to European application (EPO) 02078743.8 filed 09/03/2002. Nevertheless, the L being a single bond is not disclosed in

Art Unit: 1639

the European application or the PCT application. L is indicated, for example in claims 1 of the PCT application as being either present or absent. The examiner submits that L being a absent does not necessarily constitute a single bond.

Therefore 2/28/2005 is the date for the purposes of prior art concerning claims 15-17,20-24,27,28, 32-34.

Withdrawn Objection(s) and/or Rejection(s)

The rejection of claims 15-17,20-24,27,28 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn in view of applicant's amendments.

The rejection of claims 15,16, 20-24,27 under 35 U.S.C. 102(b) as being anticipated by Langer et al (2001 Bioconjugate Chem 12:1028-1034 – IDS entry 4/27/2007) is hereby withdrawn in view of applicant's amendments.

The rejection of claims 15,16, 20-24,27 and 17,28 under 35 U.S.C. 103(a) as being unpatentable over **Langer et al** (2001 Bioconjugate Chem 12:1028-1034 – IDS entry 4/27/2007) in view of **Dunn-Dufault et al** (2000 Nuclear Medicine and Biology 27:803-807 – IDS entry 4/27/2007) is hereby withdrawn in view of applicant's amendments.

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

Art Unit: 1639

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15,20,21,24,27 are rejected under 35 U.S.C. 102(b) as being anticipated by **Aya et al** (US Patent 3,899,472).

This rejection is necessitated by Applicant's amendment to the claims.

Claim 15 is drawn to A solid phase bound organic conjugate represented by formula

(I)

wherein the sphere is a solid phase support;

C is a carbon atom.;

R4 and R5 are independently selected from the group consisting of H, aliphatic substituents, aromatic substituents, RO, RS and (R)2N, wherein R is an aliphatic or aryl group;

L is a single bond; and

each of R1 and R2 is independently a metal coordinating group, a non-coordinating organic group, a metal coordinating group derivatized with a biologically active molecule, or a non-coordinating organic group derivatized with a biologically active molecule.

Claims 20,21,24,27 represent variations thereof.

Aya et al teach, throughout the document and especially the scheme shown embedded in columns 1 and 2, chloromethyl polystyrene derivatized with iminodiacetic acid. Said polystyrene is taken as the solid phase support of claim 15. The methyl group shown by Aya et al is taken as the carbon atom with R4 and R5 being hydrogen (elected species) of claim 15. L is a single bond to the polystyrene backbone according to Aya et al, as set forth in claim 15. R1=R2=COOH according to Aya et al which are taken as metal coordinating groups, such as set forth in claim 15.

Art Unit: 1639

Absent evidence to the contrary, said chloromethyl polystyrene derivatized with iminodiacetic acid is taken as “capable” of reacting with a solution of $[M(OH_2)_3(CO)_3]^{n+}$, as set forth in amended claim 20. Aya et teach in column 12, line 55 a flask, which is taken as the container and vessel, set forth in claims 20 and 21, respectively. Aya et al teach filtration of reaction products in column 15, lines 21-22, as set forth in claim 24.

Said $R_1=R_2=COOH$ of Aya et al is directly attached to a tertiary amine, as set forth in claim 27.

New Claim Rejection(s) – 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15, 20,21,24,27 and 16,17,28,32,33,34 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Aya et al** (US Patent 3,899,472) in view of **Dunn-Dufault et al** (2000 Nuclear Medicine and Biology 27:803-807 – IDS entry 4/27/2007)

This rejection is necessitated by Applicant's amendment to the claims.

Aya et al is relied on as above.

Aya et al do not teach: biologically active small molecules such as biotin (claims 16,28,32,33) or polyethyleneglycol-polystyrene supports (claims 17,34).

Dunn-Dufault et al teach, throughout the document and especially the title and abstract a solid-phase technique for the preparation of Technetium-99m radiopharmaceuticals comprising biotinylated peptides, such as "RP488."

Said "RP488" is taken as a biologically active small molecules, such as set forth in claims 16,28,32,33.

Dunn-Dufault teach in the last paragraph on p 804, loading of RP488 on Argogel, which is a polyethyleneglycol grafted polystyrene support, such as set forth in claims 17 and 34.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to substitute the polystyrene of Aya for the polyethyleneglycol grafted polystyrene as a support of Dunn-Dufault et al and further to introduce biotin onto the metal chelating species of Aya et al.

One of ordinary skill in the art would have been motivated to substitute the polystyrene of Aya for the polyethyleneglycol grafted polystyrene as a support of Dunn-Dufault et al and further to introduce biotin onto the metal chelating species of Aya et al

Art Unit: 1639

because it would provide the means to perform biodistribution studies, as demonstrated by Dunn-Dufault in table 1, providing important information regarding any *in vivo* labeling reagent.

Furthermore, substitution of the polyethyleneglycol grafted polystyrene support of Dunn-Dufault et al for the polystyrene of Aya et al represents substituting equivalents known for the same purpose (i.e. a resin for peptide synthesis and/or metal chelation), a basis for obviousness according to MPEP 2144.06.

One of ordinary skill in the art would have had a reasonable expectation of success in substituting the polystyrene of Aya for the polyethyleneglycol grafted polystyrene as a support of Dunn-Dufault et al and further to introduce biotin onto the metal chelating species of Aya et al because both Dunn-Dufault et al and Aya et al are concerned with metal chelation, thus the method of Dunn-Dufault et al lies well within the scope of the technology according to Aya et al.

Claims 22,23 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Aya et al** (US Patent 3,899,472) **in view of Dunn-Dufault et al** (2000 Nuclear Medicine and Biology 27:803-807 – IDS entry 4/27/2007) as applied to claims 15, 20,21,24,27 and 16,17,28,32,33,34 above, and further in view of **Alberto et al** (1998 JACS 120:7987-7988 - IDS entry 4/27/2007).

This rejection is necessitated by Applicant's amendment to the claims.

Aya et al in view of Dunn-Dufault et al is relied on as above.

Aya et al in view of Dunn-Dufault et al do not teach solutions or reagents for preparation of $[M(OH_2)_3(CO)_3]^{n+}$, such as set forth in claims 22 and 23.

Alberto et al, teach throughout the document and especially scheme 1, a solution of and the reagents necessary for the preparation of $[^{99m}Tc(OH_2)_3(CO)_3]^+$.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to place a container of reagents for the preparation of a solution of $[^{99m}Tc(OH_2)_3(CO)_3]^+$ per Alberto et al next to the flask of polyethyleneglycol grafted polystyrene based metal chelator comprising biotin according to Aya et al in view of Dunn-Dufault et al.

One of ordinary skill in the art would have been motivated to place a container of reagents for the preparation of a solution of $[^{99m}Tc(OH_2)_3(CO)_3]^+$ next to the flask of polyethyleneglycol grafted polystyrene based metal chelator comprising biotin according to Aya et al in view of Dunn-Dufault et al Dufault et al because ^{99m}Tc , as a radionuclide, is inexpensive and readily available in any hospital, according to Alberto et al on p 7987 left column second paragraph and further that $[^{99m}Tc(OH_2)_3(CO)_3]^+$ may be desirably converted into $[TcPADA(CO)_3]^+$ in one step, according to Alberto et al on p 7988 right column first full paragraph: in this vein, Alberto et al suggest in scheme 2 and p 7988 left column second full paragraph that PADA provides a group for covalent attachment of a biomolecule (i.e. such as the biotinylated peptides of Dunn-Dufault et al).

One of ordinary skill in the art would have had a reasonable expectation of success in placing a container of reagents for the preparation of a solution of $[^{99m}Tc(OH_2)_3(CO)_3]^+$ next to the flask of polyethyleneglycol grafted polystyrene based

Art Unit: 1639

metal chelator comprising biotin according to Aya et al in view of Dunn-Dufault et al Dufault et al because kits including separate flasks and containers have been successfully used in the art for some time. Furthermore, all three references concern metal chelation, thus the scope of teachings according to Alberto et al lies well within the scope of technology per Aya et al in view of Dunn-Dufault et al.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, J. Douglas Schultz can be reached on 571 272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1639

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christopher M Gross
Examiner
Art Unit 1639

cg

/Mark L. Shibuya, Ph.D./
Primary Examiner, Art Unit 1639